Basic physiological systems indicator's informative assessment for children and adolescents obesity diagnosis tasks

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Abstract. The healthcare computerization creates opportunities to the clinical decision support system development. In the course of diagnosis, doctor manipulates a considerable amount of data and makes a decision in the context of uncertainty basing upon the first-hand experience and knowledge. The situation is exacerbated by the fact that the knowledge scope in medicine is incrementally growing, but the decision-making time does not increase. The amount of medical malpractice is growing and it leads to various negative effects, even the mortality rate increase. IT-solution's development for clinical purposes is one of the most promising and efficient ways to prevent these effects. That is why the efforts of many IT specialists are directed to the doctor's heuristics simulating software or expert-based medical decision-making algorithms development. Thus, the objective of this study is to develop techniques and approaches for the body physiological system's informative value assessment index for the obesity degree evaluation based on the diagnostic findings.

1. Introduction

In 1998 the World Health Organization (WHO) mentioned obesity as a global epidemic. Nowadays it is one of the most widespread chronic conditions in the world: by the beginning of the XXI century, over 30% of the world population was overweight [1]. The major medical consequences of obesity such as the non-insulin dependent diabetes and cardiovascular diseases lead to the high disability and premature mortality rate [2-4]. Over 60% of adults has an obesity that appeared in their childhood, which is only worsening and causes the major complications [5-7]. The pediatric and adolescent obesity that is prolonged in adult life has a more severe disease course and is accompanied by a more significant weight gain and concurrent disease incidence rate than the obesity appeared at a mature age [8,9].

In 2004, the World Health Organization put forward an initiative: "The Global Strategy on Diet, Physical Activity and Health (DPAS)". The key element of this initiative is in-patient program supplemented by professional and therapeutic training aimed at the body weight reduction. Therefore, in Russia up to the present moment, there has been no targeted obesity detection programs and obesity is diagnosed lately. According to A.V. Kartelishev [10] 65% of all obese children falls on the first-degree obesity children but only 5,5% of them attend the doctor.

In 2014, the Government of the Russian Federation declared the list of top-priority research

missions [11] that require engaging all available resources. This list includes a socially significant and orphan endocrine system diseases personalized treatment development (mission №7). It is necessary to reduce the amount of obese people in Russia down to rate of 5-10%, number of non-insulin dependent diabetes cases to 3% and disability diagnosis rate resulting from endocrine system disease complications by 30-50%.

The medical research support systems came into common use not so long ago even though the theoretical studies devoted to these systems were carried out at the end of 1950s. In general, the term "decision support system" (DSS) means a computer system that can influence the decision-making processes in different branches of human activities by information acquisition and analysis. In healthcare, these systems are named as "clinical decision support systems". Studies in this field have been carried out in various directions [12-23] for 30 years. According to e-Library, the amount of publications on this subject is constantly growing in our country, mostly in the last two years.

Nowadays there are several main approaches to medical decisions support that are aimed to increase their efficiency, there is an on-line analytical processing toolkit, an algorithmic approach (pattern recognition techniques, artificial intelligence, fuzzy logic, applied mathematical statistics etc.), knowledge-based systems (datamining, expert systems) and external resource-based systems (evidence-based resource databases, doctor and patient forums). There is also a set of knowledge retrieval systems and some new software products.

Among the homegrown technologies, it is possible to mention EXNA, ACCOD, OTEKS systems (Novosibirsk), IMSLOG integrated tool set (Yankovskaya A.E., Tomsk), DeepDataDriver system (Dyuk V.A. and Aseev M.G., St. Petersburg) and General-purpose Qualifier (Yudin V.Sch., Moscow). WIZWHY system (WizSoft, USA) based on the limited search algorithms to find out some Boolean data patterns is widely used among foreign programs. There are also some widely used decision tree systems such as See5/C5.0 (RuleQuest, Australia) and statistics packages SAS (SAS Institute Company), SPSS, STATGRAPICS, STADIA, STATISTICA and etc. that have DataMining elements. BrainMaker (CSS) and OWL (HyperLogic) are popular for neural networks design. CART (USA) and PatternRecognitionWorkbench (Unica, USA) were developed for classification and regression tree system creation. Stefanyuk V.L., Osipov G.S., Averkin A.N., Fominykh I.B., Popov E.V., Pospelov D.A., Gavrilova T.A., Finn V.K., Khoroshevsky V.F., Borisov A.N., E. Mamdani and L. Zadeh, G. Klir and other scientists carried out researches on computer expert systems. N. A. Korenevsky, E. S. Podvalny, B. A. Korbinsky, O. V. Rodionov, E. N. Korovin, V. N. Frolov, D. Ferruccio, E. S. Boerner and others devoted their articles to the computer-assisted diagnosis issues. Meanwhile, the decision-making process efficiency improvement tasks during the obesity diagnosis and treatment are still relevant.

One of the main aspects while working with decision support system data is to decrease the n-dimension attribute space. To solve this problem, the indexes must be selected with respect to their informative value assessment.

2. Informative value assessment approaches

To set a diagnosis means to determine the medical condition or to make sure that it lacks. It can be done if the indexes common to this research target (patient) are obtained and analyzed properly. These indexes must be relevant and informative.

So, first of all, it is necessary to assess the index informative value and exclude the less informative indexes in order to reduce the attribute space. The index informative value depends entirely on how it helps to differentiate the condition we are concerned with. If the index can be regularly observed under different conditions, it is likely that it will not help the diagnostics and prediction. The more informative index corresponds to the greater the distance between random variables [24]. There are at least two approaches to assess the index informative value (energy and information approaches) [25].

The energy approach is based on the fact that the index informative value is assessed by the index value itself. The indexes are ordered by the magnitude and the index with the highest magnitude is considered as the most informative. For instance, during the amplitude-time analysis of ECG, the R wave amplitude is considered as the most informative index. Therefore, this approach to the

informative value assessment can be inappropriate for the object recognition tasks. In fact, if an index has high magnitude, but is almost equal for various class objects, it is almost useless for class identification tasks.

At the other hand, index with low magnitude, which is different for various object classes, it can be easily used as a classifier. It means that the information approach is more appropriate for object recognition. If the object should be ranged in class during the recognition, it is possible to use the index probability distributions difference as a significant mark. Informative value assessment $I(x_j)$ is an area of x_j index distribution that is not common with the other distribution areas of the same index.

3. Information approach

Cumulative frequency method (CFM). If there are two index samples (x) typical for two different classes, the x index empirical distributions and the cumulative frequencies (the total of frequencies from the initial one to the immediate distribution interval) can be calculated and built within the same axis. The maximum cumulative frequencies difference can be used to assess the informative value of the x index.

Shannon method suggests assessing the informative value as an average-weighted amount of data accounted for various index gradations. It describes indexe's information as the eliminated entropy value.

So, the informative value *j*-index is:

$$I(x_i) = 1 + \sum_{i=1}^{G} (P_i \sum_{k=1}^{K} P_{i,k} \cdot \log_k P_{i,k}), \tag{1}$$

where G – number of index gradations;
K – amount of classes;
P_i – probability of the *i*-th index gradation.

$$P_i = \frac{\sum_k^K m_{i,k}}{N} \tag{2}$$

$m_{i,k}$ – rate of the *i*-th gradation in the *K*-class;
N – total amount of observations;
$P_{i,k}$ – probability of the *i*-th index gradation in *K*-class.

$$P_{i,k} = \frac{m_{i,k}}{\sum_{k=1}^{K} m_{i,k}} \tag{3}$$

Kullback method is used to assess the informative value. In medicine, it is possible to deal with the diagnosis issues, establishing diagnosis and medical condition definition only when the informative indexes typical to the patient are obtained and analyzed. Thus, it is necessary to determine the most informative indexes that characterize the patients psychophysical condition. The diagnosis depends on a kind of datamining based on these indexes. There are various techniques to assess the informative value, e.g. Shannon method and the cumulative frequency method, but let us concentrate on Kullback method of informative value assessment.

Indexes informational content depends entirely on how much this index helps to differentiate the object state. The more informative index corresponds to the greater distance between the random variables. The most widespread informative value for these distances is Kullback measure [24].

In 1948, a logarithmic measure was proposed by N. Wiener and K. Shannon as a way to define the amount of information. They offered the formula that was recognized as information quantitative measure [24]. There is one measure that was introduced by Jeffreus in 1964 and was studied in detail by Kullback as an informative value $J(1,2)$, a measure of discrepancies between statistical distributions 1 and 2. For discrete distributions, this formula is as follows:

$$J(x_i / A_1, x_i / A_2) = \sum_j \lg \frac{P(x_{ij} / A_1)}{P(x_{ij} / A_2)} \left[P(x_{ij} / A_1) - P(x_{ij} / A_2) \right] \tag{4}$$

where A_1, A_2 – state classes; i –sign number; j – number of *i*-th sign range; $P(x_{ij} / A_k)$ – probability

of object hitting belonging to A_k class in the j sign range. Kullback method to determine the informative value can be presented with the following algorithm (fig. 1).
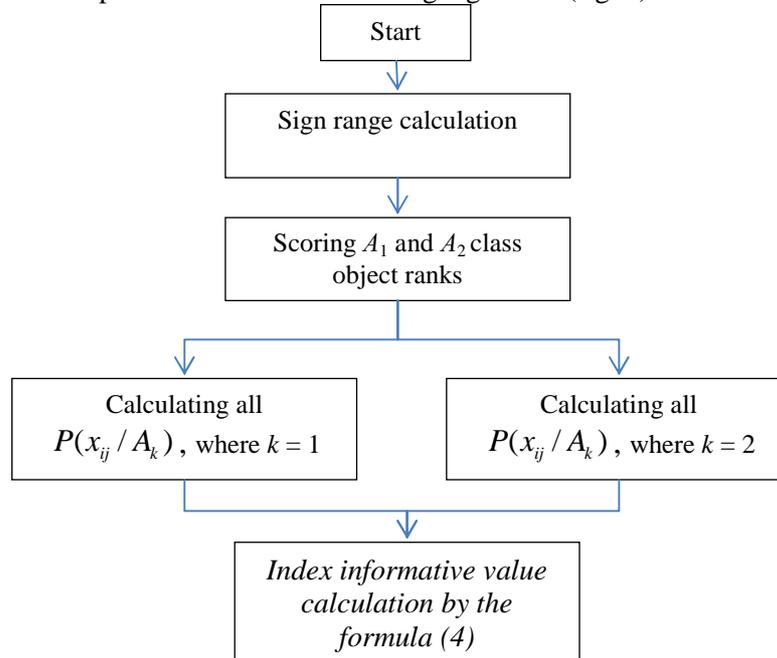

Figure 1. Kullback's informative value asessing algorithm

This criterion allows coming to conclusion on the differences of empirical aspects without any special restrictions on random distributions that form an empirical aspect. The indexes where the low informative value ranks are dominant, will have a low informative value, in other words, they will provide "correct" and "incorrect" diagnostic criteria with a close frequency. Thus, it is worth placing the indexes in a diagnostic table in an order of decreasing the informative value. Herein, the time rate of the right boundary reaching will be the highest upon the average, and the amount of mistakes will be the lowest.

To identify what contribution this index rank makes to reach the right diagnostic boundary and this is informative value J(x), it is necessary to know not only the likelihood ratio (or its logarithms) but also to take into account the probability of A1 or A2 class people to get to this rank.

The probability for some people will be determined by the number of diagnostic criteria that will bring the answer to the boundary that is correct for the majority of observations of this rank. The probability for other people will be determined by the number of diagnostic criteria that will pull the answer away from the boundary.

Table 1 shows criteria that determine the more appropriate technique to detect the index informative value for the given study:

Table 1. Comparative analysis of the index informative value assessing methods

	Index encoding degree	Number of classes	Dependence on sample size
CFM	Is sufficient	only two classes	sample size should be equal for both classes
Shannon method	Is insufficient	random number of classes	sample size can be different for different classes
Kullback method	Is insufficient	only two classes	sample size can be different for different classes

This study uses two sample types, the sample size is different for two classes and the selected technique does not depend on encoding, so it is possible to conclude that Kullback method is more appropriate to determine the index informative value.

The authors developed the NPP – a software product that uses Kullback method for informative value assessment. Programm interface is whown at figure 2 (but we have to mention that this software solution has only Russian localisation now).
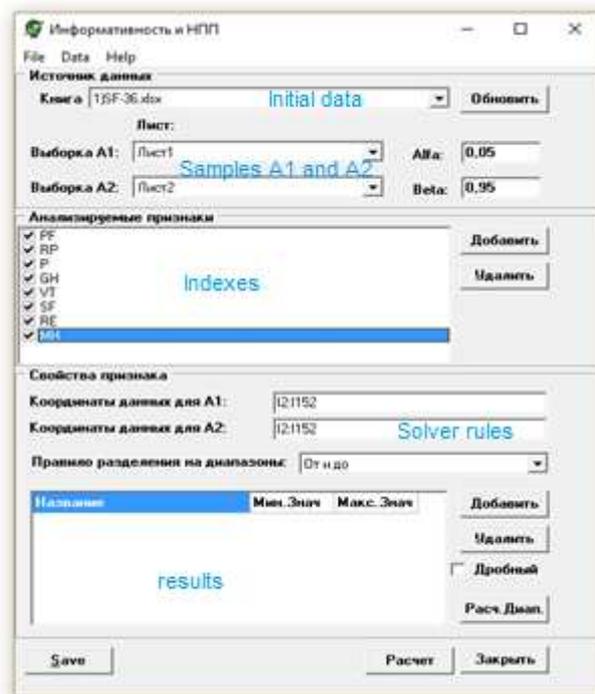
Figure 2. NPP interface

One more technique to determine the index informative value is based on its variation assessment before and after the treatment or, in other words, the change accuracy assessment.

Wilcoxon test is a statistical criterion for the sample difference assessment.

The Wilcoxon test null-hypothesis assumes the fact that compared samples distribution centers are displaced relative to each other by a certain extent. The algorithm is as follows:

- to take the first and second sample data;
- to calculate the difference of every measurement subtracting the first sample values from the second ones;
- to calculate the number of negative and positive values and to define the higher number of values as a standard change – the highest amount of changes;
- to finde the absolute differences between values;
- to range all values ignoring their sign;
- to summ up the value ranks belonging to the first group in order to get value W;
- to compare the obtained W-value with the critical value that could be expected for the null-hypothesis.

4. Research task description and solution

Tomsk Research Institute of Health Resort Study and Physical Therapy provided the following data sets: clinical findings, cardiovascular system indicators, physical efficiency, lipid metabolism, blood biochemistry, hormonal state, immunological status, blood plasma oxidation capacity and kininogenase system status (fig. 3). The data were received during the clinical studies from 2006 to 2013 and describes 464 children at the ages from 10 to 15 years suffering from obesity.
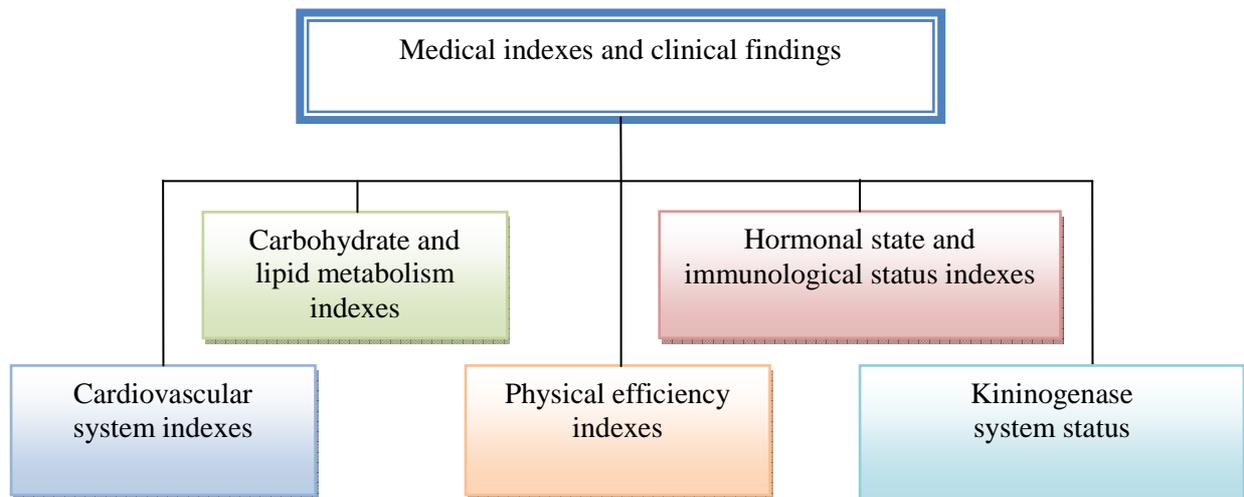
Figure 3. Sets of medical indexes

The problem can be solved based on the given data that contain the following basic indexes:

- WAIST – waist measurement;
- THIGHS – measurement round the hips;
- WEIGHT– body weight;
- EX_MASS – excess weight in %;
- IMT – body-weight index;
- SAD – systolic blood pressure;
- DAD – diastolic blood pressure;
- HOMA – insulin resistance homeostasis model assessment;
- TFN – exercise tolerance;
- WORK – performance efficiency;
- DV.PR –myocardium double oxygen saturation;
- OL – LDL-cholesterol lipids;
- TAG – triacyglyceride content in blood serum;
- OXC – total cholesterol content in blood serum;
- aXC – alpha cholesterol content in blood serum;
- LPONP – very low-density lipoproteins;
- LPNP - low density lipoproteins;
- IA – atherogenic index;
- glukoza – glycaemic level;
- T3 (1,0-2,8) – triiodothyronine content in blood serum;
- T4 (53-158) – tetra-iodothyronine content;
- TTG (0,23-3,4) – thyroid-stimulating hormone content in blood serum;
- Insylin – insulin content in blood serum;
- Kortizol – cortisone content in blood serum;
- FNO (ne >2,5 pg/ml) – tumour necrosis factor content in blood serum;
- IgA – immunoglobulin A concentration in blood serum;
- IgG - immunoglobulin G concentration;
- IgM - immunoglobulin M concentration;
- CIK – circulating immune complexes in blood serum;
- Lizocim – lysozyme activity in blood serum;
- T-lim – circulating immune complexes in blood serum;
- Txel – circulating immune complexes in blood serum;
- T-syp – circulating immune complexes in blood serum;

- B-lim – circulating immune complexes in blood serum;
- KK – kininogenase level in blood serum;
- PI – prothrombin consumption in blood serum;
- MG – macroglobulin in blood serum;
- APF – angiotensin converting enzyme in blood serum.

Mentioned indexes were studied twice: before and after the treatment, as well as their differences and changes were described. The index informative value was assessed with NPP program. Thus, the "Physical efficiency" set was defined with following indexes: exercise tolerance, performance efficiency, insulin resistance homeostasis model assessment and myocardium double oxygen saturation. The informative value of this set components is displayed in table 2.

Table 2. "Physical efficiency" indexes informative value

Index	Informative value
TFN	1,4
WORK	0,99
HOMA	0,44
DV.PR.	0,01

It is obvious, that the TFN (exercise tolerance, fig.4) is the most informative index of this set, DV.PR (fig.5) is the least informative.
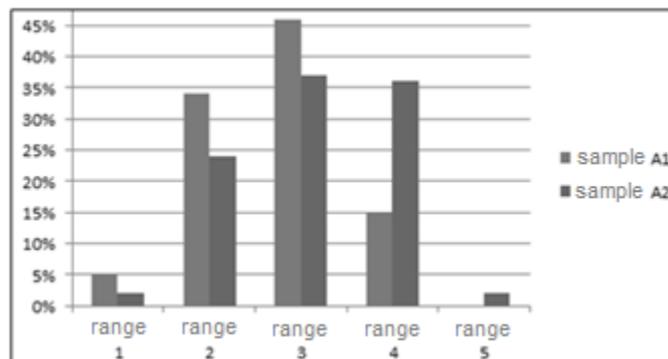

**Figure 4.** "Exercise tolerance" index
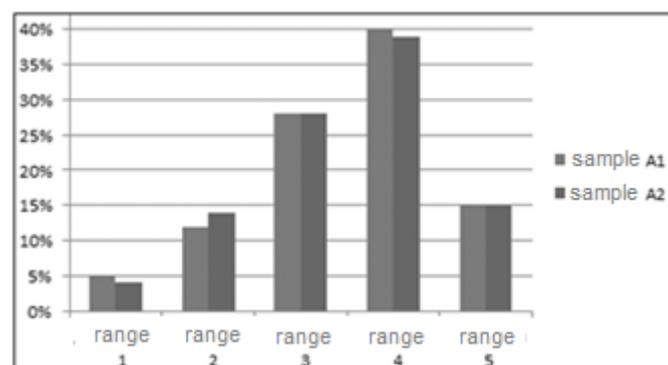
Figure 5. "Rate pressure product of myocardium oxygen saturation" index

The graphs of the most and the least informative index were built for every set. An A1 sample includes the values-before-treatment; an A2 sample consists of the values after the treatment. The bigger difference between the samples corresponds to the more informative index. Figure 4 shows that A1 sample distribution is displaced to the left side, A2 sample distribution is displaced to the right and

the difference is evident. Figure 5 shows that the difference between the samples is nonsignificant, so the index is less informative.

The change accuracy assessment was carried out based on Wilcoxon test, written in R scripting language. This language is designed for statistical data processing and allows to implement wide range of statistical procedures. Function *wilcox.test()* was used to carry out the Wilcoxon test within RStudio system (as it is shown at fig.6) [26, 27].
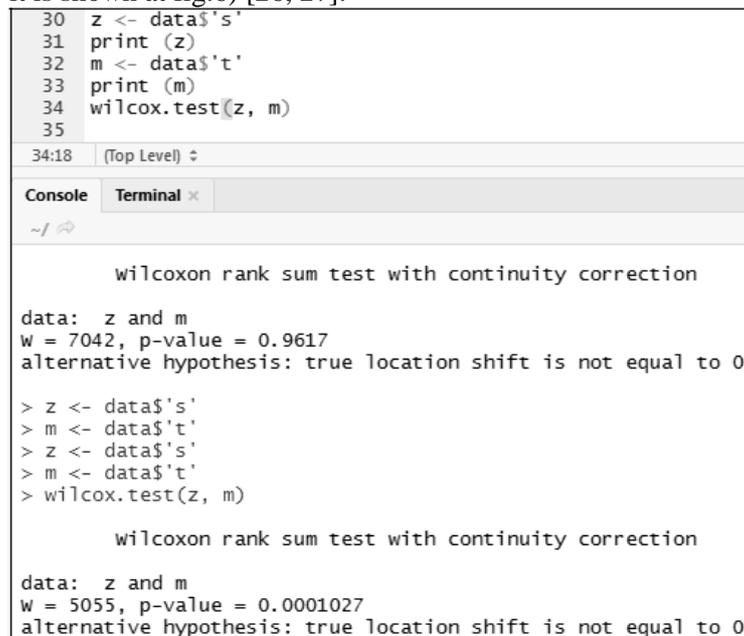
```
30   z <- data$'s'
31   print (z)
32   m <- data$'t'
33   print (m)
34   wilcox.test(z, m)
35
34:18   (Top Level) ÷

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~/ ⇨

         wilcoxon rank sum test with continuity correction

data:  z and m
W = 7042, p-value = 0.9617
alternative hypothesis: true location shift is not equal to 0

> z <- data$'s'
> m <- data$'t'
> z <- data$'s'
> m <- data$'t'
> wilcox.test(z, m)

         wilcoxon rank sum test with continuity correction

data:  z and m
W = 5055, p-value = 0.0001027
alternative hypothesis: true location shift is not equal to 0
```

Figure 6. Wilcoxon test within RStudio

Variable z is an index value before the treatment; m – an index value after the treatment. These variables were filled with data columns s (TFN before the treatment) and t (TFN after the treatment) from the "data" file that contains all given obesity indicators. Figure 6 shows the Wilcoxon test calculation for TFN index of the "physical efficiency" set.

Table 3 displays the Wilcoxon test calculation results for the "physical efficiency" set. The table uses the following symbols: W – Wilcoxon diagnostic value (it is a sum of ranks within the only one sample), p is a value that is used while statistical hypothesis testing as the null-hypothesis mistake rejection likelihood.

Table 3. Wilcoxon test

Index	W	p	Comparison with $p = 0,05$
HOMA	17070	0,2835	$p > 0,05$, the differences are statistically insignificant,
TFN	5055	0,0001	$p < 0,05$ the differences are statistically significant
DV.PR.	7042	0,9617	$p > 0,05$ the differences are statistically insignificant
WORK	1175	0,1046	$p > 0,05$ the differences are statistically insignificant

The table shows that (according to received value *p-value* = 0,00001) the TFN index before and after the treatment shows statistically significant changes, in other words, the differences are valid. The differences between other indexes samples are not significant.

5. Conclusion
As a result, the most informative indexes were determined for each data set:

- for clinical findings – lean body mass (LBM);
- for physical efficiency – exercise tolerance;
- for cardiovascular system - systolic blood pressure (SBP);
- for lipid metabolism - low density lipoprotein;
- for biochemistry of blood - alkaline phosphatase in blood serum;
- for hormonal state - interferon (not less than 45 pg/ml);
- for immunological status - circulating immune complex;
- for kininogenase system status – kininogenase level;
- for blood plasma oxidation capacity - nitrogen oxide content in blood serum.

When Wilcoxon test was calculated, the following results were obtained: for the clinical finding – sample differences, body mass index and a lean body mass differences were statistically significant. For the physical efficiency – only an exercise tolerance index has a significant value, for the cardiovascular system – diastolic and systolic blood pressure, lipid metabolism – low density lipoprotein. For blood biochemistry and hormonal state sets all indexes differences were statistically insignificant. The immunological status – significant circulating immune complexes in blood serum and immunoglobulin A concentration in blood serum. For kininogenase system status and oxidation capacity of blood plasma sets, the authors obtained the results that $p<0,05$ for all indexes, so the differences between the samples are statistically significant.

I n general the results are also similar for other two methods. Thus, the informative indexes were selected based on the given sample. The research data will be used to develop the Tomsk Research Institute of Health Resort Study and Physical Therapy knowledge database and an intelligent clinical decision support system.

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